Heredity in insanity

Eugenics Record Office

BULLETIN No. 3

PRELIMINARY REPORT OF A STUDY OF HEREDITY IN INSANITY IN THE LIGHT OF THE MENDELIAN LAWS

BY

GERTRUDE L. CANNON, A.M.

AND

A. J. ROSANOFF, M.D.

KINGS PARK STATE HOSPITAL, KINGS PARK, NEW YORK

Reprinted from
JOURNAL OF NERVOUS AND MENTAL DISEASE
Vol. 38, No. 5, pp. 272–279, 1911

COLD SPRING HARBOR, N. Y.
May, 1911

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By Gertrude L. Cannon, A.M., and A. J. Rosanoff, M.D.

KINGS PARK STATE HOSPITAL, NEW YORK

Insane hospital statistics show plainly that heredity has much to do with the causation of certain forms of nervous and mental disease. Yet we know but little of the exact conditions under which such disease is transmitted from parent to offspring. The object of the present research has been to accumulate and examine such data as may serve to throw some light upon this obscure problem.

It has been shown that the laws governing the transmission of traits by heredity, as established by Mendel, hold good not only for plants and the lower animals, but also for man, at least as regards certain characters, such as color of hair and color of eyes. In view of this fact our problem has assumed for us a more definite form. It is simply: Are any of the forms of nervous and mental disease transmitted from generation to generation in accordance with the Mendelian laws?

§ 1. *The Mendelian Laws.*—Perhaps a brief review of the essential points of the Mendelian laws will not be superfluous.

The total inheritance of an individual from his parents is divisible into unit characters, each of which is inherited independently of all the rest and may therefore be studied without reference to other characters.

The inheritance of any such character is believed to be dependent upon the presence in the germ plasm of a unit of substance called a *determiner.*

With reference to any given character the condition in an individual may be *dominant* or *recessive:* the character is dominant when, depending upon the presence of its determiner in the germ plasm, it is plainly manifest; and it is recessive when, owing to the lack of its determiner in the germ plasm, it is not present in the individual under consideration.

The dominant and recessive conditions of a character are often designated by the symbols D and R, respectively.

To make the matter clearer, we may take as an example of a Mendelian character the case of eye color.

The brown color is the dominant condition, while the blue color is the recessive condition, as was shown by Davenport.[1] It would seem that the inheritance of brown eyes is due to the presence in the germ plasm of a determiner upon which the formation of brown pigment in the anterior layers of the irides depends.

On the other hand, the inheritance of blue eyes is believed to be due to the lack of determiner for brown eye pigment in the germ plasm; for the blue color of eyes is due merely to the absence of brown pigment, the effect of blue being produced by the choroid coat shining through the opalescent but pigment-free anterior layers of the irides in such cases.

It must be borne in mind that as regards the condition of any character every person inherits from two sources, namely, from each parent. Therefore, with reference to any character he may be pure bred or hybrid.

A case of inheritance of a character from both parents is spoken of as one of *duplex inheritance* and is often designated by the symbol DD.

A case of inheritance of a character from only one parent is spoken of as one of *simplex inheritance* and is designated by the symbol DR.

A case in which a character is not inherited from either parent, therefore exhibiting the recessive condition, is spoken of as one of *nulliplex inheritance* and is designated by the symbol RR.

We are now in a position to estimate the relative number of each type of offspring according to theoretical expectation in the case of any combination of mates.

There are but six theoretically possible combinations of mates. Continuing to make use of the case of eye color as an instance of a Mendelian character, let us consider in turn each theoretical possibility.

1. Both parents blue-eyed (nulliplex): all children will be blue-eyed, as may be shown by the following biological formula: $RR \times RR \infty RR$.

2. One parent brown-eyed and simplex (that is to say, inherit-

[1] Science, N. S., Vol. XXVI, Nov. 1, 1907, pp. 589-592.

ing the determiner for brown eye pigment from one parent only), the other blue-eyed: half the children will be brown-eyed and simplex and the other half blue-eyed: $DR \times RR \infty DR + RR$.

3. One parent brown-eyed and duplex, the other blue-eyed: all the children will be brown-eyed and simplex: $DD \times RR \infty DR$.

4. Both parents brown-eyed and simplex: one-fourth of the children will be brown-eyed and duplex, one-half will be brown-eyed and simplex, and the remaining one-fourth will be blue-eyed (nulliplex): $DR \times DR \infty DD + 2DR + RR$.

5. Both parents brown-eyed, one duplex the other simplex: all the children will be brown-eyed, half duplex and half simplex: $DD \times DR \infty DD + DR$.

6. Both parents brown-eyed and duplex: all the children will be brown-eyed and duplex: $DD \times DD \infty DD$.

It will be readily seen from these formulæ that in attempting to predict the proportions of the various types of offspring that may result from a given mating it is necessary to know, not only whether the character is in each parent dominant or recessive, but in the case of the dominant condition also whether it is duplex or simplex.

Turning again to the case of eye color, an individual with blue eyes we know to be nulliplex, as he has no brown pigment in his eyes and therefore could not have inherited the determiner for brown eye pigment from either parent. But how are we to judge in the case of a brown-eyed person whether he has inherited the determiner for that character from both parents or only from one? We can judge this only by a study of the ancestry and offspring of the individual.

To put the whole matter in a nutshell, the essential difference between a dominant and a recessive condition of a character is in the fact that in a case of simplex inheritance the dominant condition is plainly manifest, while the recessive condition is not apparent and can be known to exist only through a study of ancestry and offspring.

This is important because it constitutes the criterion by which we are able to determine whether any given inherited peculiarity or abnormality is, as compared with the average or normal condition, dominant or recessive.

§ 2. *General Survey of Material.*—We may now proceed with the examination of our material, which consists of the pedigrees

of eleven patients at this hospital and includes thirty-five different matings, with a total of 221 offspring. This material has been arranged for convenience in the form of pedigree charts.

One of the first facts that appeared in the study of the pedigrees was that any form of insanity or even all the forms of hereditary insanity do not constitute an independent hereditary character, but that they are closely related to imbecility, epilepsy, hysteria, and various mental eccentricities that are not usually included under the designation insanity. In other words, the distinction between these conditions as clinical entities cannot, in the light of their manner of origin, be regarded as deeply essential.

We find as manifestations of the neuropathic make-up in closely related persons cases of feeble-mindedness, convulsions in childhood from trivial causes or chronic epilepsy, cases of grave hysteria, various eccentricities, cases of dementia præcox, manic-depressive insanity, paranoic conditions, involutional psychoses, and the like.

It is not to be assumed, however, that what we have called here the neuropathic make-up constitutes the basis of all the clinical forms of nervous and mental disease; for on the one hand, some of these conditions, like general paresis or alcoholic polyneuritis, are probably purely exogenous in origin, and, on the other hand, others, like Huntington's chorea, are plainly independent Mendelian characters.

The pedigree charts contain a number of instances of neuropathic children born of normal parents, but not a single instance of a normal child born of parents both of whom are neuropathic.

This proves that the neuropathic make-up cannot be dominant over normal; but that if its transmission occurs at all in a manner corresponding to the Mendelian laws, it must be recessive to normal.

In preparing the pedigree charts we have made use of the following symbols and abbreviations.

□ = male individual. O = female individual. A square or a circle unmarked = normal individual. P = normal individual with neuropathic offspring. I = insanity. Cv. = convulsions. E = epilepsy. N = feeble-mindedness, hysteria, or other pronounced neuropathic manifestation. o within a square = normal individual without offspring. † = died in childhood. ? = data unascertained.

Number above each mating indicates type of combination.

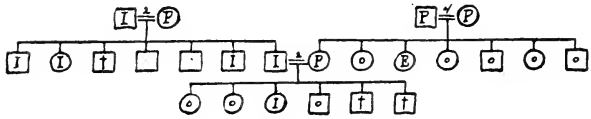
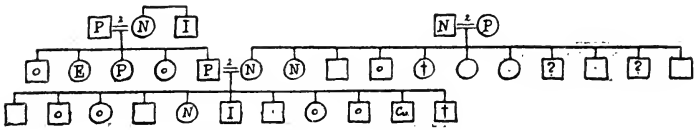


CHART I. L. R. Case No. 4215



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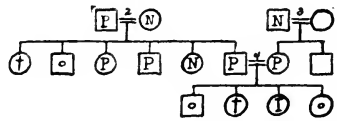

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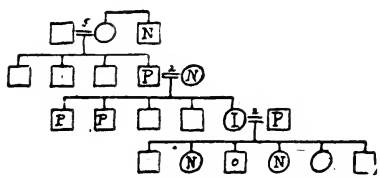

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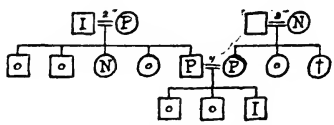

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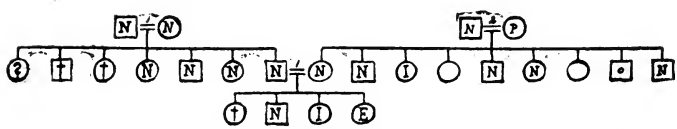


CHART VI. E. R. H. Case No. 455

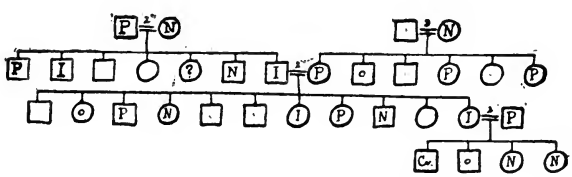


CHART VII. L. W. Case No. 14840

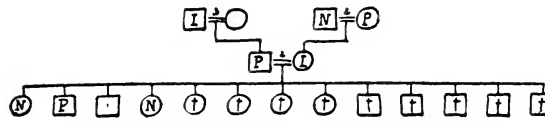
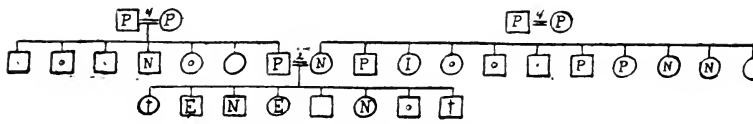


CHART VIII. M. E. S. Case No. 4455



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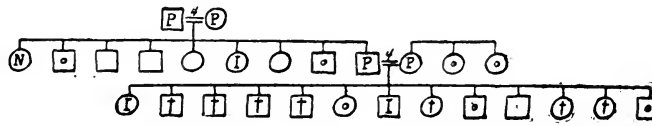

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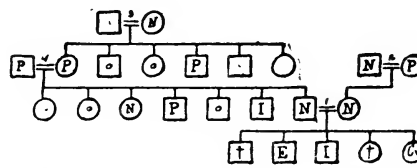

CHART XI. C. R. S. Case No. 17242

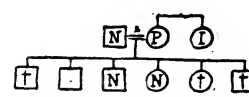

CHART XII. C. R. S.'s step-brothers and step-sisters.

§ 3. *Analysis of Pedigrees.*—Let us now compare the proportions of normal and neuropathic offspring which have resulted from the different matings, as shown in the pedigree charts, with the proportions of theoretical expectation. This will enable us to determine whether or not the neuropathic make-up is actually transmitted in the manner of a recessive condition of a Mendelian character. In other words, let us test, with the aid of our material, the hypothesis that the neuropathic make-up is due to a lack of a determiner in the germ plasm upon which the normal function of the nervous apparatus depends.

We may consider the matings in the order of the six theoretical possibilities discussed in the first part of this paper.

The first combination, RR × RR ∞ RR, is represented in our pedigree charts by three matings with a total of 16 offspring. Theoretically all the offspring of such matings should be neuropathic. The charts show that 10 were neuropathic, 5 died in childhood, and data concerning the remaining one are wanting.

The second combination, DR × RR ∞ DR + RR, is represented in our pedigree charts by nineteen matings with a total of 129 offspring. Theoretically one-half of these should be neuropathic and one-half normal, but capable of transmitting the neuropathic make-up to their progeny. The charts show: 45 neuropathic, 14 normal with neuropathic offspring, 20 normal without offspring, 27 normal with normal offspring, 20 died in childhood, and concerning 3 data were unascertained.

The third combination, DD × RR ∞ DR, is represented in our pedigree charts by five matings with a total of 18 offspring. Theoretically all the offspring of such matings should be normal but capable of transmitting the neuropathic make-up to their progeny. The charts show: 8 normal with neuropathic offspring, 7 normal with normal offspring, 2 normal without offspring, and 1 died in childhood.

The fourth combination, DR × DR ∞ DD + 2DR + RR, is represented in our pedigree charts by seven matings, with a total of 54 offspring. Theoretically one-fourth of these should be neuropathic, one-half normal but capable of transmitting the neuropathic make-up to their progeny, and the remaining one-fourth normal and not capable of transmitting the neuropathic make-up to their progeny. Our charts show: 12 neuropathic, 6 normal with neuropathic offspring, 10 normal with normal offspring, 18 normal without offspring, and 8 died in childhood.

The fifth combination, DD × DR ∞ DD + DR, is represented in our pedigree charts by only one mating, with 4 offspring. Theoretically all the offspring should be normal, half of them should and half should not be capable of transmitting the neuropathic make-up to their progeny. The chart shows that all were normal, one had neuropathic offspring, the rest had normal offspring.

The sixth combination, DD × DD ∞ DD, is not represented in our charts. This combination constitutes the mating of normal individuals of pure normal ancestry, and should produce only normal offspring. Since we have investigated the pedigrees of

neuropathic subjects it is not surprising that we have found no instance of such a mating in our material.

§ 4. *Theoretical Expectation.*—We have seen that in our material the correspondence between theoretical expectation and actual findings is very close. That is to say, the hypothesis according to which the neuropathic make-up, as here defined, is recessive to normal, in the Mendelian sense, is borne out by the facts as shown in our pedigrees.

Should larger accumulations of such data in the future give similar results, we shall be able to establish the following rules of theoretical expectation.

1. Both parents being neuropathic, all children will be neuropathic.

2. One parent being normal, but with the neuropathic taint from one parent, and the other parent being neuropathic, half the children will be neuropathic and half will be normal, but capable of transmitting the neuropathic make-up to their progeny.

3. One parent being normal and of pure normal ancestry and the other parent being neuropathic, all children will be normal but capable of transmitting the neuropathic make-up to their progeny.

4. Both parents being normal but each with the neuropathic taint from one parent, one-fourth of the children will be normal and not capable of transmitting the neuropathic make-up to their progeny, one-half will be normal but capable of transmitting the neuropathic make-up, and the remaining one-fourth will be neuropathic.

5. Both parents being normal, one of pure normal ancestry and the other with the neuropathic taint from one parent, all the children will be normal, half of them will be capable and half incapable of transmitting the neuropathic make-up to their progeny.

6. Both parents being normal and of pure normal ancestry, all children will be normal and not capable of transmitting the neuropathic make-up to their progeny.

In concluding this report, we wish to acknowledge with gratitude our indebtedness to Dr. Charles D. Davenport, of the Carnegie Institution of Washington, for his guidance, advice and assistance in this work.

DISCUSSION

AT NEW YORK NEUROLOGICAL SOCIETY, OCTOBER 4, 1910.

Prof. Charles B. Davenport, of the Carnegie Institution, Washington, D. C., said that in considering the reasons why the data presented in the paper read by Dr. Rosanoff offered a decided advance over those that had been collected before, we must recognize the fact that there were two principal methods employed by the authors of this paper that had not been employed hitherto, and which were responsible for the results obtained. The first of these was the new method of collecting the data concerning inheritance. Hitherto, such information had been obtained largely from parents or guardians, the questioning being usually limited to asking these relatives whether there were any similar cases of nervous disease in the family. The result of such questioning was usually negative, apparently because under the conditions of the inquiry, the parents or guardians were not inclined to state the exact facts. In consequence of this, the patient's family history, as gathered in the hospital, has little value, a fact that has been generally recognized by those engaged in this work.

The method of collecting data which was employed by Miss Cannon and Dr. Rosanoff has been quite different. In their work, an attempt was made to employ the best scientific methods: *i. e.,* to find out what the exact facts were at whatever cost of time and expense. A person biologically trained and trained in the rapid diagnosis of mental disease visits the family to which the patient belonged, and enters into such a cordial relation with the members of that family that the mother, for example, soon becomes quite willing to tell the truth, whereas, if she were brought before the hospital officials she might hesitate or decline to tell the facts. In addition to this, the field worker, who is not limited as to the time and expense in her attempts to learn the facts, can visit other members and branches of the family; she can see the family physician and the neighbors in order to corroborate the statements made by the parents or wards. By this method, in the course of time, the field worker obtained the real facts in the case, and such a history, when compared with that usually obtained in the hospital, clearly demonstrated the total inadequacy of the latter.

The method of obtaining a fuller and more satisfactory family history in cases of insanity has been adopted in the study of other mental defects and diseases. The school for Feeble Minded at Vineland, N. J., now employs four of these field workers, and as the results of their investigations they are getting to a point where they begin to realize that none of these cases of feeblemindedness or imbecility are isolated; that all of them have arisen from an ancestry which on both sides is neuropathic. Epilepsy is being studied in the same way in the State institutions for the care of such patients at Skillman, N. J., and Palmer, Mass., where they have, in each case, one worker in the field, and only recently those in charge of the Crocker Cancer Fund of the Columbia University have decided to adopt the same plan in studying the family history of those who suffer from cancer.

The second advance in the paper of Miss Cannon and Dr. Rosanoff relates to the method of studying the data they have collected. Hitherto, in studying the data of these cases, it had been considered impracticable

to get the law of inheritance from a single family, and the practice had been to lump the data, and say, for example, that in one hundred cases of insanity, a distinct inheritance was found in 35. This method of lumping the data had not been generally satisfactory, and of no practical use in predicting what would be the outcome of the children of a particular mating, nor was it of any particular value in explaining how a particular insane patient came to exist. The present method avoided this massing of the data by boldly attacking each family, and recognizing that the insanity was due to a particular combination of maternal and paternal germ-plasms. This gave an entirely different value to the study of heredity and enabled us to say that a particular mating would necessarily give rise to such and such a proportion of insane offspring, or that a certain insane patient must have had insanity in both the maternal and paternal germ-plasms.

One remarkable fact that had been brought out was the close relationship between different forms of amentia—dementia præcox, manic-depressive insanity, senile dementia do not depend on the absence of different kinds of units. The same rules of inheritance held good for epilepsy and feeblemindedness, namely, that two feeble-minded parents could have only feeble-minded offspring, and that two epileptic parents could have only feeble-minded or epileptic offspring. Many of the statistics which had been collected hitherto did not bear, as they had been thought to bear, upon the question of causation of these various mental defects. For example, statistics had been collected upon the alcoholic habits of the parents, upon their nutritional defects and clinical history, but we now knew that no matter under what conditions the children were born, whether under favorable or unfavorable conditions, the statistical results remained practically constant and the same.

As to the relation between heredity and environment, the question was often asked, did the latter play any part at all in determining the onset of mental disease? In the case of the feeble-minded it seemed that environment did play a small part: in the case of insanity, a larger part. Both environment and the neuropathic condition of the protoplasm were active factors in the production of insanity. An unfavorable environment, falling upon an individual with an inherited weakness, resulted in a mental breakdown. The result was always due to the combination of the environment and the protoplasm. The disease itself was not inherited; only the weakness, and the disease made its appearance only when some stress of life fell upon such a weak protoplasm. Then the protoplasm showed its weakness, and the individual succumbed.

Dr. B. Onuf said the valuable paper of Drs. Cannon and Rosanoff, while largely theoretical, had also practical aspects. Any one of us might be confronted with the question of whether, under given conditions of ancestry, certain persons should contract marriage. Naturally, our answer to such a question had usually been quite vague. If the investigations made by the authors of this paper, which he understood was only a preliminary report, were corroborated by further statistics, then our knowledge of heredity would become clearer and better defined and enable us to give correspondingly clearer answers to the inquiries mentioned.

Dr. Onuf referred to the fact that certain psychoses seemed to occur within well-defined lines. Thus, manic depressive insanity was very apt to occur in families, and paranoid conditions on the other hand were often associated with an ancestral history of paranoid disease. Certain types of convolutions had been found to occur in succeeding generations.

The speaker said it was very important to establish clearly the relation between neuropathic and psychopathic heredity. That was also a point of which we knew very little. Some writers would include suicide in the list of psychopathic heredity; others apoplexy, others chorea, and so on. We should define what factors were of importance in psychopathic and what in neuropathic heredity. It had been shown, for example, that normal persons showed a stronger heredity as regarded apoplexy than did insane ones, so that apoplexy, as an etiological factor in insanity, lost much of its meaning.

Dr. Rosanoff, in closing the discussion, agreed with Dr. Davenport as to the methods which contributed to the value of the data presented, namely, the employment of "field workers" to collect such data, and the application of the Mendelian laws in their interpretation rather than their treatment by ordinary statistical methods.

As to the role played by environment, Dr. Rosanoff thought that the results of heredity studies did not exclude factors of environment from the etiology of mental disease, but rather added evidence to show their importance. In the material which formed the basis of the paper, practical findings did not correspond exactly with theoretical expectation, and the excess over expectation was always on the side of normal offspring. It would seem that the neuropathic makeup was a character which presented shades of variation as numerous as those in the depth of brown eye color, hair color, etc. While in some instances the neuropathic makeup was so well marked as to be plainly manifest from birth, in others it consisted of nothing more than an undue lack of mental balance which resulted in attacks of insanity consequent upon comparatively trivial causes, such as, for instance, childbirth, a moderate indulgence in alcohol or some psychical shock.

As to the question raised by Dr. Onuf, namely, what diseased conditions of the nervous system shall be regarded as manifestations of the neuropathic character which was transmissible by heredity, the speaker thought Dr. Onuf was right in suggesting that conditions exogenous in origin should be excluded, and that apoplexy was in all probability one of these conditions.

The Eugenics Record Office

Cold Spring Harbor, Long Island, N. Y.

ESTABLISHED in connection with the Eugenics Section of the American Breeders Association in 1910, this office aims to fill the need of a clearing-house for data concerning "blood lines" and family traits in America. It is accumulating and studying records of physical and mental characteristics of human families to the end that the people may be better advised as to fit and unfit marriages. It issues blank schedules (sent on application) for the use of those who wish to preserve a record of their family histories.

The Eugenics Section and its Record Office are a development from the former committee on Eugenics, comprising well-known students of heredity and humanists; among others Alexander Graham Bell, Washington, D. C.; Luther Burbank, Santa Rosa, Cal.; W. E. Castle, Harvard University; C. R. Henderson, University of Chicago; Adolf Meyer, Johns Hopkins University; J. Arthur Thomson, University of Aberdeen; H. J. Webber, Cornell University; Frederick A. Woods, Harvard Medical School. The work of the Record Office is aided by the advice of a number of technical committees.

The chairman of the Section is David Starr Jordan; its secretary is C. B. Davenport. The superintendent of the Eugenics Record Office is H. H. Laughlin, Cold Spring Harbor, N. Y., to whom correspondence may be addressed.

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